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For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING SAME

(57) Abstract: Nucleic acid (e.g., DNA) hybridization probes are described which comprise a labeled, single copy nucleic acid which hybridizes to a deduced single copy sequence interval in target nucleic acid of known sequence. The probes, which are essentially free of repetitive sequences, can be used in hybridization analyses without adding repetitive sequence-blocking nucleic acids. This allows rapid and accurate detection of chromosomal abnormalities. The probes are preferably designed by first determining the sequence of at least one single copy interval in a target nucleic acid sequence, and developing corresponding hybridization probes which hybridize to at least a part of the deduced single copy sequence. In practice, the sequences of the target and of known genomic repetitive sequence representatives are compared in order to deduce locations of the single copy sequence intervals. The single copy probes can be developed by any variety of methods, such as PCR amplification, restriction or exonuclease digestion of purified genomic fragments, or direct synthesis of DNA sequences. This is followed by labeling of the probes and hybridization to a target sequence.



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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/15674

**A. CLASSIFICATION OF SUBJECT MATTER**IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/02, 21/04  
US CL : 435/6, 91.2; 536/23.1, 23.5, 24.1, 24.2, 24.3, 24.31, 24.33

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.2; 536/23.1, 23.5, 24.1, 24.2, 24.3, 24.31, 24.33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 6,222,029 B1 (EDWARDS et al) 24 April 2001, columns 21, 25-27, 31-32 and 49-50.	1-15, 17-33, 41-43
X	US 6,040,140 A (CROCE et al) 21 March 2000, column 9.	1-9, 11-13, 15-21, 23-33, 41-45
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Y		10, 14, 22
X	US 5,811,231 A (FARR et al) 22 September 1998, columns 6, 7 and 25.	1, 2, 5-14, 17-33, 41-43
Y	US 5,721,098 A (PINKEL et al) 24 February 1998, column 31.	10, 14, 22



Further documents are listed in the continuation of Box C.



See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-33, drawn to probes, methods of making probes and hybridization methods of using probes.

Groups 2-151, claim(s) 34-38, drawn to nucleic acids selected from the group consisting of SEQ ID NO: 429-446 and 480-613, respectively. For example, if group 2 is elected, then claims 34-38 will be examined to the extent that they are limited to nucleic acids consisting of SEQ ID NO: 429. Upon election of one of the groups, please specify the SEQ ID NO corresponding to the requested group.

Group 152, claim(s) 39-43, drawn to a method of identifying a previously unknown repeat sequence.

Group 153, claims 44 and 45, drawn to a method of determining a chromosome breakpoint using 2 single copy probes.

The inventions listed as Groups 1-153 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Pursuant to 37 C.F.R. 1.475(d), this Authority considers that where multiple products and processes are claimed, the first recited product, method of making the product and method of using the product shall constitute the Main Invention. Further, pursuant to 47 C.F.R. 1.475(d), it considers that any subsequently recited products and methods do not share a special technical feature with the main invention or any such other inventions. In addition, it is noted that each of the nucleic acids of groups 2-151 are distinct from one another and do not share a special technical feature because each nucleic acid consists of a unique nucleotide sequence and thereby each nucleic acid hybridizes to distinct regions of the genome and each nucleic acid has a distinct functional activity. Furthermore, the methods of groups 152 and 153 do not share the same technical feature because each method has a different objective, involves performing different method steps and utilizes different reagents (i.e., the method of group 153 requires the use of 2 probes which hybridize to opposite sides of a breakpoint, whereas the method of group 152 requires the use of a single probe and requires determining whether said probe hybridizes to at least 3 regions of the genome).

### Continuation of B. FIELDS SEARCHED Item 3:

WEST:US, EP, JP, WO Patents; DIALOG: Medline, CA, BIOSIS, EMBASE, SCISEARCH

search terms: single-copy, repeat sequences, repeat-free, blocking nucleic acids, breakpoint, translocation